Review Article

Flavonoids: A Potential Group of Phytoconstituents against Mycobacterial Infections

Naira Nayeem1*, Mohd Imran1, Abdulhakim Bawadekji2

(Received 26/02/2018; accepted 17/04/2018)

Abstract: Phenolic compounds form one of the main classes of secondary metabolites. Flavonoids constitute one of the most important groups of plant phenolics. Several flavonoids are reported to possess various activities, such as antioxidative, wound healing, hepatoprotective, antibacterial, anti-viral, anti-inflammatory, and anticancer. They are classified as flavanes, flavones, flavanols, flavanones, flavonols, flavonolignans, isoflavones, isoflavonones, chalcones and anthocyanins, depending on their structural differences, which are known for their antitycobacterial activity. Mycobacterial diseases like leprosy, tuberculosis, bovine tuberculosis, paratuberculosis, etc., are caused by a member of the Actinobacteria family. Mycobacterial infections are chronic due to the composition of the cell wall and their adaptability and hence can survive in different habitats for years. The control of these diseases is a challenging task in several ways. A plethora of data is available on the plants which have been screened for their antitycobacterial activity. Some of them report the active phytoconstituents while others report the mechanisms of action of these phytoconstituents. Furthermore, many researches have evaluated and reported the anti-mycobacterial activity of the extract containing flavonoids and fractions of plants extracts rich in flavonoids. In this paper, an attempt is made to summarize and highlight the plants that have been evaluated for anti-mycobacterial activity, the various mechanisms of action, the various flavonoids involved and their biological sources.

Keywords: Flavonoids; Antimycobacterial; Phytoconstituents; Extracts; Secondary metabolites.

1658-7022© JNBAS. Published by Northern Border University (NBU). All Rights Reserved.

*Corresponding Author: :

(1) * Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Northern Border University, P.O. Box 840, Rafha 91911, Kingdom of Saudi Arabia.
e-mail: nurah.akml@nbu.edu.sa & naira_64@yahoo.co*

(2) Deanship of Scientific Research, Northern Border University, P.O. Box 1321, Arar 91431, Kingdom of Saudi Arabia.
e-mail: srd3@nbu.edu.sa & hakimbawadekji@gmail.com

DOI: 10.12816/0046700
بحث مرجعي:
الفلافونويدات: مجموعة كامنة من المركبات النباتية المضادة للإصابات ببكتيريا الدرن (المايوكوبكتيرية)

نيرة نعيم، عبدالحميد، على بواديكي

(قدم للنشر في 05/06/2014، وقبل للنشر في 02/1439هـ)

ملخص الدراسة:
تشكل المركبات الفينولية أحد أهم منتجات الأمور الثانوية للخلايا النباتية، وتشكل الفلافونويدات مجموعة من أشهر المنتجات. وهناك العديد من الفلافونويدات التي تمتلك خصائص أو نشاطات متعددة كالشلاب المضاد للأكسدة وشفاء الجروح وحماية الكبد والتشنجات النباتية وغيرها، وكذلك إنتاج الضادات والأمراض، وتشكل الفلافونويدات المذكورة نشاط مهم على الفلافونويدات والكبد، والتشنجات، والنفايات، والأمراض الأخرى. تتألف الفلافونويدات بشكل عام من الفلافونات والكربونات والأنزيمات والأمراض المتزامنات، والأنثوسكانيات، والتسلسل النباتي، وتشكل بعض الفلافونويدات المضادة للأمراض للأمراض المتزامنة، إن هذه الأمراض كمرض السكري والسرطان والมะوس والفيروسبائية وتشكل الصناعات الفلاحية. يتبع نشاط الفلافونويدات المضادة للأمراض الميكروبكتيرية تأثيرات تختلف في النطاقات المختلفة، وتتأثر الفلافونويدات المضادة للأمراض الميكروبكتيرية باستخدام تقنيات متنوعة.

الكلمات المفتاحية:
الفلافونويدات: مضادات الميكروبكتيرية، المركبات النباتية، مستخلصات النباتية، مركبات الأمور الثانوية

المراجعات:
(1) قسم الكيمياء، كلية مكتبة الصيدلة، جامعة الحدود الشمالية، ص.ب. 840، رفحاء 91911، المملكة العربية السعودية.
   e-mail: nurah.akml@nbu.edu.sa & naira_64@yahoo.co
(2) عرعش البحث العلمي، جامعة الحدود الشمالية، ص.ب. 1321، عرعش 91431، المملكة العربية السعودية.
   e-mail: srd3@nbu.edu.sa & hakimbawadekji@gmail.com

DOI: 10.12816/0046700

50014-11658-7022

qrtba@journals.nbu.edu.sa
http://jnbas.nbu.edu.sa
1. INTRODUCTION

Nature is the important source of medicinal plants having bioactive principles. The last few years have seen a surge of interest in herbas as they are considered to be safe and more dependable when compared to synthetic drugs which are expensive and may possess various side effects. The phytoconstituents present in plants have been reported to possess various activities, some of them being anti-oxidant, antimicrobial, anthelmintic, etc. Furthermore, there is a large scope for research in the field of herbal medicines as traditional knowledge can be utilized for the development of drugs of medicinal importance (Chew, Jessica, & Sasidharan, 2012; Vinayaka, Nandini, Rakshitha, Martis, Shruthi, Hegde, Prashith, & Raghavendra, 2010).

Mycobacteria are pathogens that cause a range of mycobacterioses in humans and animals. Due to the composition of their cell walls and ability to adapt to their habitat they can survive for years. Mycobacterial diseases are caused by a member of the Actinobacteria family. Mycobacterial infections like leprosy, tuberculosis etc are chronic diseases and hence it is challenging to control these diseases. Symptoms of diseases are fever, weight loss and fatigue. There are several mycobacterial species like Mycobacterium leprae, Mycobacterium tuberculosis, Mycobacterium smegmatis Mycobacterium bovis etc. Several important antibiotics have originated from plant products and have received considerable attention as potential anti-mycobacterial agents. Many other compounds that have been reported and proven to be of use as leads for newer drugs for treatment of Tuberculosis (TB) have been obtained from the natural sources (Nguta, Appiah-Opong, Nyarko, Yeboah-Manu, Addo, Otchere, & Kissi-Twum, 2016).

From time immemorial traditional herbs have been enormously used in various regions of the world for treating mycobacterial diseases. Lately, efforts have been made by various researchers to probe and investigate the knowledge obtained about herbal medicines from traditional healers from different parts of the world. It has been reported that secondary metabolites of plants can affect the microbial cell in several ways. They may bring about a change in membrane function, interfere with the process of Deoxyribonucleic Acid (DNA) replication and Ribonucleic Acid (RNA) transcription, they may disrupt protein synthesis and coagulation of cytoplasmic contents and to a certain extent interrupt the gene regulation and quorum sensing (Radulović, Blagojević, Stojanović-Radić, & Stojanović, 2013).

A significant amount of literature is available which report the resistance of bacteria to the effects of the antibiotic. Hence, plant based medicine is being implemented in recent times as therapy for anti-mycobacterial diseases; so as to decrease the occurrence of these infections in humans as well as animals, (Tiwari, Chakraborty, Dhama, Rajagunalan, & Singh, 2013). Plants serve as the main source of natural compounds as a result of their vast biodiversity. Plant secondary metabolites like alkaloids, flavonoids, phytosterols, saponins, tannins etc. have been screened for anti-mycobacterial properties. Flavonoids consist of a group of polyphenolics that contain a benzo-γ-pyrene ring structure and are synthesized by phenylpropanoid pathway. The literature reports several studies indicating the effects of flavonoids against microbial infections and certain non-communicable diseases i.e. cardiovascular diseases, cancers, and other age-related diseases.

The structure of flavonoids consists of a fifteen-carbon skeleton inclusive of two benzene rings linked by a heterocyclic pyran ring. They can be divided into a variety of classes based on the variations in the structure; such as flavones, flavonols, flavanones, anthocyanidines, flavans, flavonolignans, isoflavones, isoflanonanes, and chalcones (Pandey, 2007; Cook & Samman, 1996; Rice-Evans, Miller, Bolwell, Bramley, & Pridham, 1995).

The activities and chemical nature of flavonoids depend on the structure, pattern of hydroxylation, polymerization, conjugations and substitutions...
It has been reported that for a significant antitubercular activity, if the positions C-5 and C-7 are substituted with hydroxyl group there is loss of activity while hydroxyl group at C-5, C-6, C-7 or C-3 and C-4 are important for activity (Paragas, Gehle, Krohn, Franzblau, & Macabeo, 2014). Furthermore, another important aspect has been reported with reference to the structure activity relationship of the flavonoid i.e. O-methylation i.e. methylation at the oxygen atom or glycosylation at any of the hydroxyl substitutions inactivates the anti-tubercular activity of the flavonoids (Yadav, Thakur, Prakash, Khan, Saikia, & Gupta, 2013).

The objective of this review article is to highlight and to outline the biological origin of flavonoids that have been evaluated for their anti-mycobacterial activity along with their mechanisms of action.

2. MECHANISM OF ACTION OF FLAVONOIDS

Flavonoids exhibit a number of pharmacological and anti-bacterial activities. Flavonoids harm the bacterial cells in various ways like their ability against microbial adhesins, cell-wall or transport proteins restriction activation in drug metabolism etc. (Kumar & Pandey, 2013).

The general chemical structures of different classes of flavonoids are as shown in Figure (1). The literature review reports several mechanisms of action of flavonoids in mycobacterium species. These compounds effectively inhibit the targets which are important for the growth and virulence. Scientists have reported that flavonoids have the ability to inhibit the enzyme

![General structure](Image)

![Flavan-3-ol](Image)

![Anthocyanidin](Image)

![Flavone](Image)

![Isoflavone](Image)

![Flavonol](Image)

![Flavanone](Image)

Figure 1: The chemical structures of different classes of flavonoids
Rv0636 which is present in the fatty acyl synthase complex II (Brown, Papaemmanouil, Bhowruth, Bhatt, Dover, & Besra, 2007). Myricetin and quercetin-3-O-β-D-glucoside were isolated from the aqueous extract of Pelargonium reniforme and have been reported to increase the intracellular uptake of mycobacterium by macrophages and thereby bringing about the removal of bacilli (Kim, Griffiths, & Taylor, 2009). Fushiya et al have reported that the flavone 5,4′-Dihydroxy-6,7,8,3′-tetramethoxyflavone isolated from the methanolic extract of Cleome droserifolia suppressed the nitric oxide production and decreased the oxidative stress in activated macrophages (Fushiya, Kishi, Hattori, Batkhuu, Takano, Singab, & Okuyama, 1999).

Currently, research is being focused by various researchers to throw light on the various mechanisms of action of flavonoids in inhibiting Mycobacteria (Ramachandran & Balasubramanian, 2014). Various mechanisms of the flavonoids against mycobacteria reported in the literature are as depicted in Table (1).

**Table 1:** Mechanism of action of certain flavonoids.

<table>
<thead>
<tr>
<th>S. No</th>
<th>Compounds</th>
<th>Mechanism</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Chrysin - flavone</td>
<td>Effective inhibitors on multidrug transporters</td>
<td>(Tran, Marks, Duke, Bebawy, Duke &amp; Roufogalis, 2011).</td>
</tr>
<tr>
<td>2</td>
<td>Genistein - isoflavone</td>
<td>Effective inhibitors on multidrug transporters</td>
<td>(Jaganathan, 2011).</td>
</tr>
<tr>
<td>3</td>
<td>Isoliquiritigenin, Butein</td>
<td>Inhibit the fatty acid synthase II responsible for mycolic acid synthesis</td>
<td>(Brown, Papaemmanouil, Bhowruth, Bhatt, Dover, &amp; Besra, 2007).</td>
</tr>
<tr>
<td>4</td>
<td>Quercetin</td>
<td>Toprim domain of subunit B of</td>
<td>(Suriyanarayanan, Shannmugam, 2013).</td>
</tr>
</tbody>
</table>

3. ANTIMYCOBACTERIAL ACTIVITY

3.1 Anti Mycobacterial Activity of Plant Extracts

It has been reported that when the individual isolated compound is tested at a particular concentration it is often less active than the whole plant itself, which may imply that crude plant extracts may be exerting their activity through synergistic or additive effect (Wagner & Ulrich-Merzenich, 2009). Hence, many plant extracts containing flavonoids (in the preliminary
phytochemical investigation) / flavonoid rich fractions have been investigated for their antimycobacterial activity by various groups of researchers. Most of the literature reported the anti-mycobacterial activity against Mycobacterium tuberculosis H37Rv, while a few reported activity against other mycobacterial species.

3.2 Anti Mycobacterial Activity of Plant Extracts against Mycobacterium Tuberculosis

Mycobacterium tuberculosis H37Rv strain was used to evaluate aqueous extracts i.e. Rhoeo Spathacea, Centella asiatica, Annona muricata, Pluichea indica, and Andrographis paniculata. The results revealed that Pluichea indica, and Rhoeo spathacea showed the best activity when compared to the other extracts (Radji, Kurniati, & Kiranasari, 2015). The activity of petroleum ether, ethyl acetate, and methanol extracts of Stachys thirkei, Stachys ttmolea, Thymus sibthorpii, Satureja aintabensis, Ballota acutabulosa and Micromeria Juliana was reported in another study. The extracts containing favonoids i.e., T. sibthorpii, S. aintabensis, and M. juliana developed significant activity against M. tuberculosis with the minimum inhibitory concentration of 12.5-100 μg/ml. (Askun, Tekwu, Satil, Modanligolu, & Aydeniz, 2013). The petroleum ether extract and chloroform extract of Leucas marrubioides exhibited significant activity against M. tuberculosis (Gowrish, Vagdevi, & Rajashekar, 2015). The crude ethanolic extract of the Morinda citrifolia fruits was subjected to a preliminary qualitative screening of phytoconstituents which revealed the presence of flavonoid, scopoletin, anthraquinone and alkaloids. The anti-mycobacterial activity was attributed to these constituents (Novie, Mauliku, Hendro, Suharyo, & Tri, 2017). The methanolic extracts of the seeds of Peganum harmala were reported to exhibit significant activity and this was attributed to the flavonoid content of the plant (Davoodi, Ghaemi, Mazandarani, Shakeri, Javid, & Klishadi, 2015). Several other plants have been evaluated for their antimycobacterial effect some of them are as follows Euphorbia hirta (Rajasekar, Anbarasu, Manikkam, Joseph, & Kumar, 2015), Acalypha indica, Allium cepa, Allium sativum, Adhatoda vasica and Aloe vera.

All plants showed good antimycobacterial activity (Gupta, Thakur, Singh, Singh, Sharma, Katoch, & Chauhan, 2010), Quercus infectoria, Citrus aurantium, Caesaphilium pulcherima, Mimosa pudica, Mentha spicata and Chysanthemum parthenium (Sheeba, Gomathi, & Citarasu, 2015). Eucalyptus camaldulensis, Ocimum basilicum, Calpurnia aura, Artemisia abysinica, Croton macrostachyus (Gemechu, Giday, Worku, & Ameni, 2013), Cissampelos owariensis (Rebecca, Koma, Ibrahim, & Otu, 2013), Glycyrrhiza glabra (Nair, Pharande, Bannalikar, & Mukne, 2015), Syzygium aromaticum, Aegle marmelos, Glycyrrhiza glabra, Piper nigrum and Lawsonia inermis. (Kaur & Kaur, 2015), Rubia cordifolia (Makghato, Nxumalo, Ndaba, Masilo, Tsindane, & Sedibane, 2017) Artemisia afra, Dodonea angustifolia, Drosera capensis and Galenia africana against Mycobacterium smegmatis (Mativandelda, 2008). A study by Khlifi et al. who have evaluated the activity of G. alypum leaves have reported the presence of anthocyanins, polyphenols, flavonoids and tannins in methanolic and petroleum ether extracts. The petroleum ether extract was particularly active against M. tuberculosis. (Khlifi, Hamdi, El Hayouni, Cazaux, Souchard, Couderc, & Boujila, 2011).

The methanolic extracts of nine plants i.e. Salvadora persica, Accacia senegal, Acokanthera friesianum, Plumbago daviei, Loranthus accacia, Cordia sinensis, Acacia horrida, Albizia anhelmitica and Euphorbia scarlatica were evaluated against the M. kansasii, M. tuberculosis, M. smegmatis, M. fortuitum. The extracts of S. persica and C. sinensis exhibited antituberculosis activity against M. tuberculosis and M. kansasii (Richard, Callistus, Nick, & Paul, 2010).

3.3 Anti Mycobacterial Activity of Plant Extracts against Mycobacterium Lapreae

Very little data is available about plants being evaluated for the activity against Mycobacterium
lapreae. Review reports the use of Humulus japonicas, Calliandra portoricensis, Cassia nigricans, Manilkara hexandra, and Bauhinia variegate for the treatment of Mycobacterium lapreae was due to the presence of flavonoids (Gadekar, Singour, Chaurasiya, Pawar, & Patil, 2010).

3.4 Anti Mycobacterial Activity of Plant Extracts against other Mycobacteria

The flavonoid and alkaloid fractions Dioscorea oppositifolia, Corallocarpus epigaeus, Dioscorea bulbifera, Dioscorea hispida, Dioscorea pentaphylla, Amorphophyllus sylvaticus, Andrographis paniculata, Morinda citrifolia, Enicostema axillare, Gloriosa superba were screened for their activity against two mycobacteria i.e. M. smegmatis and M. phlei. The results revealed that the chloroform extract of A. paniculata was most effective growth inhibitor of M. smegmatis. (Rajesh & Archana, 2017) i.e., methanol, n-hexane and dichloromethane of rhizomes of Zingiber officinale and Curcuma longa were evaluated for mycobacterial activity against Mycobacterium abscessus, Mycobacterium smegmatis, Mycobacterium phlei and Mycobacterium fortuitum. The methanol and n-hexane extracts of Curcuma longa showed the highest zone of inhibition for M. abscessus (Ogudo, Lawal, & Adeniyi, 2014).

3.5 Anti Mycobacterial Activity of Isolated Flavonoids

The literature review also reports the antimycobacterial activity of several isolated flavonoids. The antimicrobial activity of the ethyl acetate extract of Argyreia speciosa was reported by Habbu et al. This activity was attributed to quercetin 3′7 di-O methyl 3-sulphate and kaempferol 7-O methyl 3-sulphate which was found to be synergistic with the usual antimycobacterial agents (Habbu, Mahadevan, Shastry, & Manjunatha, 2009). The methanolic extract of Bromelia balansae showed moderate activity and the various flavonoid glycosides identified from this extract were kaempferol-3-O-α-L-rhamnopyranosyl, quercetin-3-O-α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside, kaempferol-3-O-α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside, and kaempferol 3,7-di-O-α-L-rhamnopyranoside (Coelho, Honda, Vieira, Brum, Pavan, Leite, & Cardoso, 2010).

The review reveals that most of the flavonoids active against mycobacteria belong to the classes of flavones and flavonones. Some of the flavonoids that have been reported to be responsible for the antimycobacterial activity are as depicted in Table (2). The table also gives information regarding the botanical source, chemical class and the mycobacteria. The structures of some of the isolated compounds that have exhibited activity against mycobacteria are as shown in Figures (2-20).

Table 2: Flavonoids responsible for the antimycobacterial activity.

<table>
<thead>
<tr>
<th>S. No</th>
<th>Chemical Class</th>
<th>Botanical Source</th>
<th>Phytoconstituent</th>
<th>Mycobacteria</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Flavonoid</td>
<td>Dorstenia barteri (Moraceae)</td>
<td>isobavachalcone, kanzanol C, 4-hydroxylchonocarpin, stipulin, amentoflavone</td>
<td>M. tuberculosis, M. smegmatis</td>
<td>(Kuete, Ngameni, Mbaveng, Ngadjui, Meyer, &amp; Lall, 2010).</td>
</tr>
</tbody>
</table>
Table 2 (Cont.)

<table>
<thead>
<tr>
<th>S. No</th>
<th>Chemical Class</th>
<th>Botanical Source</th>
<th>Phytoconstituent</th>
<th>Mycobacteria</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Cinnamolyglico Flavonoids</td>
<td>Heritiera littoralis (Sterculiaceae)</td>
<td>3-cinnamoyltribuloside</td>
<td>M. madagascariense M. indicus pranii. (Christopher, Nyandoro, Chacha, Koning, 2014).</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Flavonoids</td>
<td>Spordinias mombin (Anacardiaceae)</td>
<td>mombincone, and mombinol</td>
<td>M. tuberculosis</td>
<td>(Olugbuyiro, &amp; Moody, 2013).</td>
</tr>
<tr>
<td>5</td>
<td>Flavanone</td>
<td>Dasymaschalon dasymaschalum (Annonaceae)</td>
<td>7-hydroxy-6,8-dimethoxyflavanone</td>
<td>M. tuberculosis</td>
<td>(Prawat, Chairek, Lenthas, Salae, &amp; Tuntiwachwuttikul, 2013).</td>
</tr>
<tr>
<td>7</td>
<td>3-hydroxyisoflavonoes</td>
<td>Dalbergia melanoxylon (Fabaceae)</td>
<td>kensanone F 7 methyl ether</td>
<td>M. tuberculosis</td>
<td>(Mutai, Heydenreich, Thoithi, Mugumbate, Chibale, &amp; Yenesew, 2013).</td>
</tr>
<tr>
<td>8</td>
<td>Flavone</td>
<td>Galenia Africana (Aizoaceae)</td>
<td>(2S)- 5, 7, 2’-trihydroxy flavanone</td>
<td>M. tuberculosis</td>
<td>(Mativandlela, 2009).</td>
</tr>
<tr>
<td>9</td>
<td>Flavone</td>
<td>Ocimum sanctum (Lamiaceae)</td>
<td>Luteolin</td>
<td>M. tuberculosis</td>
<td>(Birdi, D’Souza, Tolani, Daswani, Nair, Tetalib, Toroc, &amp; Hoffnerc, 2012).</td>
</tr>
<tr>
<td>10</td>
<td>Biflavonoids</td>
<td>Garcinia livingstonei (Clusiaceae)</td>
<td>Amentoflavone and 41monomethoxy amentoflavone</td>
<td>M. smegmatis</td>
<td>(Kaikabo &amp; Eloff, 2011).</td>
</tr>
<tr>
<td>11</td>
<td>Isoflavone Flavanone</td>
<td>Ficus nervosa (Moraceae)</td>
<td>genistein prunet (O-methylated isoflavone), and (2S)-naringenin</td>
<td>M. tuberculosis</td>
<td>(Chen, Cheng, Peng, &amp; Chen, 2010).</td>
</tr>
<tr>
<td>12</td>
<td>Flavones</td>
<td>Limnophila geoffroyi (Scrophulariacea e)</td>
<td>nevadensin isothymusin</td>
<td>M. tuberculosis</td>
<td>(Suksamrarn, Poomsing, Aroonerk, Punjanon, Suksamrarn, &amp; Kongkun, 2003).</td>
</tr>
</tbody>
</table>
### Table 2 (Cont.)

<table>
<thead>
<tr>
<th>S. No</th>
<th>Chemical Class</th>
<th>Botanical Source</th>
<th>Phytoconstituent</th>
<th>Mycobacteria</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>Flavonoids</td>
<td><em>Pelargonium reniforme</em> (Geraniaceae)</td>
<td>myricetin and quercitin-3-O-β-d-glucoside</td>
<td><em>M. tuberculosis</em> <em>M. fortuitum</em></td>
<td>(Kim, Griffiths, &amp; Taylor, 2009).</td>
</tr>
<tr>
<td>15</td>
<td>Trihydroxy flavanone</td>
<td><em>Pisonia aculeate</em> (Nyctaginaceae)</td>
<td>Pisonianone</td>
<td><em>M. tuberculosis</em></td>
<td>(Wu, Peng, Chen, &amp; Tsai, 2011).</td>
</tr>
<tr>
<td>17</td>
<td>Prenylated flavones</td>
<td><em>Artocarpus altiss</em> (Moraceae)</td>
<td>cycloartocarpin artocarpin cudraflavone B cudraflavone C</td>
<td><em>M. tuberculosis</em></td>
<td>(Boonphong, Baramee, Kittakoop, &amp; Puangsombat, 2007).</td>
</tr>
<tr>
<td>19</td>
<td>Flavanones</td>
<td><em>Chromolaena odorata</em> (Asteraceae)</td>
<td>isosakuranetin (5,7-dihydroxy-4'-methoxyflavanone)</td>
<td><em>M. tuberculosis</em></td>
<td>(Suksamrarn, Chotipong, Suaisom, Sriphota, Chindaduang, Chuprjob, &amp; Suksamrarn, 2009).</td>
</tr>
<tr>
<td>20</td>
<td>Flavone Flavanones Isoflavones</td>
<td><em>Butea monosperma</em> (Fabaceae)</td>
<td>7,3',4'-trihydroxyflavone four, (-)-butin, (-)-butrin, (+)-isomonospermoside and (-)-liquiritigenin, formononetin, aformosin</td>
<td><em>M. tuberculosis</em></td>
<td>(Chokchaisiri, Suaisom, Sriphota, Chindaduang, Chuprjob, &amp; Suksamrarn, 2009).</td>
</tr>
<tr>
<td>21</td>
<td>Flavone</td>
<td><em>Couroupita guianensis</em> (Lecithydaceae)</td>
<td>5,4'-Dihydroxy-3,7,8,3'-tetramethoxyflavone</td>
<td><em>M. tuberculosis</em></td>
<td>(Aravind, Karthikeyan, &amp; Babu, 2017).</td>
</tr>
</tbody>
</table>
Table 2 (Cont.)

<table>
<thead>
<tr>
<th>S. No</th>
<th>Chemical Class</th>
<th>Botanical Source</th>
<th>Phytoconstituent</th>
<th>Mycobacteria</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>Flavone</td>
<td><em>Larrea tridentate</em> (Zygophyllaceae)</td>
<td>5,4′-dihydroxy-3,7,8-trimethoxyflavone 5,4′-dihydroxy-3,7,8,3-tetramethoxyflavone</td>
<td><em>M. tuberculosis</em></td>
<td>(Favela, García, Garza, Rivas, &amp; Camacho, 2012).</td>
</tr>
<tr>
<td>27</td>
<td>Flavanone</td>
<td><em>Campomanesia adamantium</em> (Myrtaceae)</td>
<td>5,7-dihydroxy-8-C-methylflavanone 7-hydroxy-5-methoxy-6-C-methylflavanone 5,7-dihydroxy-6-C-methylflavanone 2′,4′-dihydroxy-6′-methoxychalcone, 5,7-dihydroxy-6,8-di-C-methylflavanone</td>
<td><em>M. tuberculosis</em></td>
<td>(Pavan, Leite, Coutinho, Honda, Cardoso, Vilegas, Leite, &amp; Sato, 2009).</td>
</tr>
</tbody>
</table>

**Figure 2:** The chemical structure of amentoflavon.  
**Figure 3:** The chemical structure of luteoline.
Figure 4: The chemical structure of genistein.

Figure 5: The chemical structure of prunetin.

Figure 6: The chemical structure of naringenin.

Figure 7: The chemical structure of myricetin.

Figure 8: The chemical structure of biochanin A.

Figure 9: The chemical structure of artocarpin.

Figure 10: The chemical structure of pisonianone.

Figure 11: The chemical structure of cudraflavone.

Figure 12: The chemical structure of nevadensin.
4. CONCLUSION

Flavonoids with their widespread occurrence, diversity and vast array of biologically active compounds can prove to be indispensable moities for further development and design of novel therapeutic agents for mycobacterial infections. In this review an attempt was made to give an insight into the structural aspects, the plants and the individual isolated constituents that have shown promising anti-mycobacterial activity against the various tested mycobacteria and the various probable mechanisms of action of the flavonoids. The data also suggest that the flavones and flavonones were the class of flavonoids that have exhibited significant antimycobacterial activity. It is evident from the review that most of the data that is available is for *Mycobacterium tuberculosis*. There is a
ACKNOWLEDGEMENTS

The authors are thankful to the Dean of Faculty of Pharmacy and the Deanship of Scientific Research of Northern Border University for their support during the preparation of this paper.

REFERENCES


